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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,472	04/25/2005	Gerard Griffioen	50304/068001	5411
21559	7590	02/05/2009		
CLARK & ELBING LLP 101 FEDERAL STREET BOSTON, MA 02110			EXAMINER JOKE, MICHELE K	
			ART UNIT 1636	PAPER NUMBER
			NOTIFICATION DATE 02/05/2009	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

### Office Action Summary

**Application No.**

10/527,472

**Applicant(s)**

GRIFFIOEN ET AL.

**Examiner**

MICHELE K. JOIKE

**Art Unit**

1636

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 14-23 is/are pending in the application.
- 4a) Of the above claim(s) 22 and 23 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-8508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Receipt is acknowledged of a reply to the previous Office Action, filed November 7, 2008. Claims 14-23 are pending, and claims 14-21 under consideration in the instant application. Claims 22 and 23 are withdrawn. Any rejection of record in the previous Office Action, mailed August 7, 2008 that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14, 16-18, 20 and 21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 2006/0068472 in view of Madeo et al.

Claim 15 stands rejected under 35 U.S.C. 103(a) as being unpatentable over US 2006/0068472 in view of Madeo et al as applied to claims 14, 16-18, 20 and 21 above, and further in view of Poleev et al.

Claim 19 stands rejected under 35 U.S.C. 103(a) as being unpatentable over US 2006/0068472 in view of Madeo et al as applied to claims 14, 16-18, 20 and 21 above, and further in view of White et al.

These rejections are maintained for reasons of record.

**Response to Arguments Concerning Claim Rejections – 35 USC § 103 (a)**

Applicants' arguments filed on November 7, 2008 have been fully considered.

The following grounds of traversal are presented:

US 2006/0068472 ('472) suggests a therapy where caspases are inhibited. Such therapy is performed by providing caspase inhibitors to a patient; not by inactivating a caspase gene such that a patient lacks a functional caspase. Moreover, the passage relied upon by the Office, alone or in combination with other passages of the '472 publication, does not suggest a yeast cell with amyloidogenic proteins wherein a caspase is inhibited. The Office provides no reason as to why a skilled artisan would make particular modifications to either a yeast cell described in the '472 publication or to Madeo's yeast cell to achieve the claimed yeast cell.

The '472 publication, at best, teaches that inhibiting caspases in a therapeutic context would reduce the toxicity of fragmented amyloidogenic proteins. Applicant surprisingly found that inhibition of expression of a caspase gene in yeast causes the toxic effects of amyloidogenic proteins to be more pronounced, which allows for an easier phenotypic reading of the heterologously expressed amyloidogenic protein.

Applicant's surprising finding that yeast cells in which expression of a caspase gene is inhibited causes the toxic effects of amyloidogenic proteins to be more pronounced rebuts any prima facie case of obviousness. A skilled person in search of a yeast strain where the toxicity of a heterologously expressed amyloidogenic protein is more pronounced would not be guided by the teaching of the '472 publication and, consequently, would not be motivated to combine the teachings of the '472 publication and Madeo because the '472 publication suggests reduced toxicity of amyloidogenic proteins when caspases are inhibited.

Applicant's traversal has been fully considered and found not to be persuasive for the following reasons.

Applicants are arguing that '472 reference is teaching therapy by providing caspase inhibitors, but not by inactivating a caspase gene. Applicants are claiming a yeast cell lacking a functional caspase gene. This is a broad limitation and includes, inactivating the gene, but is not limited to that. Other ways of limiting the function of the gene can be used, for example, the use of caspase inhibitors. '472 teaches that yeast cells can be used. Combined with Madeo, they teach a yeast cell with amyloidogenic proteins wherein the cell lacks a functional caspase. US 2006/0068472 teaches a host cell transformed with a gene encoding an amyloidogenic protein, and states that determining the mechanisms of toxicity of misfolded proteins (amyloidogenic proteins are toxic) remains the most important unresolved research problem for neurodegenerative diseases. Furthermore, although a yeast strain lacking a functional

caspase gene is not taught by '472, the reference teaches inhibiting caspase function. Madeo teaches a yeast strain with a disrupted YCA1 (caspase) gene. It would have been obvious to a person of ordinary skill in the art to use a disrupted caspase yeast strain because '472 teaches inhibiting capsase function, so it would naturally follow to disrupt the caspase gene to yield the predictable result of lack of function of the caspase gene.

'472 only "suggests" reduced toxicity of amyloidogenic proteins when caspases are inhibited when a mutant alpha-synuclein is used. The argument of unexpected results is not found persuasive for this reason. It is unknown how toxicity would be affected if a non-mutated amyloidogenic protein was used. The mutation itself could be affecting toxicity of the protein. There was no other indication that toxicity will be reduced when capsases are inhibited.

***Allowable Subject Matter***

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 10:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/  
Primary Examiner, Art Unit 1636

Michele K Joike  
Examiner  
Art Unit 1636

Application/Control Number: 10/527,472  
Art Unit: 1636

Page 7